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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,146	12/10/2001	Jay Cunningham	3078/04	7806

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EXAMINER
SPIVACK, PHYLLIS G

ART UNIT	PAPER NUMBER
1614	6

DATE MAILED: 03/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No. 10/016,146	Applicant(s) Cunningham et al.
	Examiner Phyllis G. Spivack	Art Unit 1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-13* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

The undersigned Examiner supports the goal of the Office to advance prosecution as expediently as is reasonably possible. Cooperation is requested with respect to the timely submission of any references deemed pertinent to the present application along with Form PTO-1449.

Claims 1-13 are presented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 C FR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C FR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C FR 3.73(b).

Claims 1-13 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6,372,719. Although the

conflicting claims are not identical, they are not patentably distinct from each other because of overlapping subject matter. Instant claim 5 does not recite "sensitive to the combination", nor does instant composition claim 9 recite "enhanced" as in claim 13 of the patent.

Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claim 1 provides for the use of compounds of the formula depicted in the claim, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 1 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for providing an additive effect following the administration of compound XII with cyclophosphamide to treat M21 human melanoma, does not reasonably provide enablement for the practice of treating or preventing any neoplasia disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to prepare and to practice the invention commensurate in scope with these claims.

At issue are both whether or not one skilled in the art could practice methods of treating any neoplastic disease, and also, whether or not one skilled in the art could prevent a neoplastic disease, comprising administering a combination of a compound of the formula of the claims with a known chemotherapeutic agent without undue experimentation, in view of the guidance provided by the disclosure and what is well known in the art. The determination of what constitutes undue experimentation in any given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art.

Factors to be considered in determining whether a disclosure would require undue experimentation include the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims.

In the instant case the state of the art is highly unpredictable and unreliable with respect to conclusions drawn from laboratory data extrapolated to clinical efficacy. Accordingly, analysis of the above criteria would lead one skilled in the art to the reasonable conclusion that undue experimentation would be required to practice the claimed methods. Particularly in view of the absence of data sufficient to support the breadth of claims 1 and 5, and the high degree of unpredictability in the art, the instant specification is insufficient to support prevention of any neoplastic disease.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rogers et al., US. Patent 6,013,651 and Remington's Pharmaceutical Sciences.

Rogers teaches various compounds of the present claims for use in the treatment of neoplastic diseases. See column 10, line 27, and columns 58-59. Further, motivation to combine other active ingredients is provided on column 10, line 20. Remington discloses, in particular, two established anti-neoplastic agents, cyclophosphamide and fluorouracil. Although neither reference alone suggests the specific combination of the other, in view of the two references, one skilled in the oncology art would have been motivated to prepare a pharmaceutical composition comprising the compounds disclosed by Rogers with cyclophosphamide or fluorouracil. Such would have been obvious in the absence of evidence to the contrary because both are well established in the prior art as anti-neoplastic agents.

It is generally *prima facie* obvious to use in combination two or more ingredients that have previously been used separately for the same purpose. In re Kerkhoven 205 USPQ 1069.

Specific statements in the references that would spell out the claimed invention are not necessary to show obviousness since questions of obviousness involve not only what references

expressly teach, but what they would collectively suggest to one of ordinary skill in the art. It would have been reasonable to expect an additive advantage of the combined agents in the treatment for neoplastic disease.

No claim is allowed.

Any inquiry concerning this communication should be directed to Phyllis Spivack at telephone number 703-308-4703.

March 21, 2003

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER